DESSERTATION
ON

A CLINICAL AND DIAGNOSTIC STUDY OF

EPILEPSY IN ADULTS

M.D. DEGREE EXAMINATION

BRANCH I

(GENERAL MEDICINE)

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INTRODUCTION

Epilepsy is the most common primary disorder of brain, and according to World Health Organization (WHO), second only to depression as the leading cause of neuropsychiatry disability worldwide. The causes and manifestations of epilepsy are so diverse and multifaceted that it impinges on virtually every aspect of modern biomedical science, from molecular biology to vocational rehabilitation.

In practice, it is useful to consider the etiologies of epilepsy based on the age of the patient, as age is one of the most important factors determining both the incidence and likely causes of epilepsy. During neonatal period and early infancy, potential causes include perinatal hypoxia, intracerebral hemorrhage and trauma, acute CNS infection, metabolic disturbances, genetic and developmental disorders.

The most common seizures arising in late infancy and early childhood are febrile seizures. During the period of childhood and adolescence, many of the well defined epileptic syndromes present like temporal lobe epilepsies, absence epilepsies, benign childhood epilepsy with Centro temporal spikes, etc., Most of these epilepsies are idiopathic and have typical EEG abnormalities and do not require further investigation.

But most of the seizures with adult onset have identifiable etiologies like neurological disorder or metabolic abnormalities. So adult onset seizures should be carefully evaluated to identify an underlying etiology. This study on “Epilepsy in adults” focused on careful clinical examination and diagnostic evaluation of patients aged more than 25 years who presented with seizures. The diagnostic tests used in this study were blood biochemical study, CT imaging of brain and Electroencephalogram (EEG).

ISTORICAL REVIEW

Epilepsy is as old as mankind. About 3000 years ago, a secondarily generalized major seizure was fully described in Akkadian, the oldest written language. Other ancient case histories were found in Egypt from 1600 BC and in India from about 1000 BC. The first known book on epilepsy was **"ON THE SACRED DISEASE",** written about 2400 years ago in the "Hippocratic school". The author is not known but is referenced as Hippocrates.He attributed epilepsy to brains having an abnormal consistency caused by superfluity of phlegm.

At the turn of seventeenth century, physical and biological sciences emerged. Luigi Galvani, the founder of field of electrophysiology, opened the gate toward understanding epilepsy by his monumental discovery of animal electricity. At the end of nineteenth century, Golgi and Ramon found the nature of connections between nerve cells. Pavel first described experimentally induced seizures recorded by electroencephalography in 1912 in Russia.

In 1929,Dr.Hans Berger, a professor of psychiatry in Germany published his discovery that spontaneous brain electrical activity in humans could be recorded from the scalp. He reported that interictal EEG changes were known in epilepsy and later he recorded human spike and wave activity. In a research EEG laboratory setup at Boston city Hospital in 1934, Gibbs, Davis and Lennox first demonstrated spike and wave complexes interictally and during clinical absences. The first use of closed circuit television (CCTV) for simultaneous recording of the EEG and seizures was reported in 1966 by Goldensohn.

REVIEW OF LITERATURE

Epilepsy is not a specific disease or even a single syndrome, but rather a broad category of symptom complexes arising from any number of disordered brain functions that they may be secondary to a variety of pathological process.

DEFINITIONS

SEIZURE[4]

A seizure is a paroxysmal event due to abnormal, excessive, hyper synchronous discharges from an aggregate of central nervous system neurons. It is manifested by stereotyped alterations in behaviour, ranging from dramatic convulsive activity to experiential phenomena not readily discernible by an observer.

EPILEPSY

A condition in which a person has recurrent unprovoked seizure due to a chronic, underlying process. Two or more recurrent unprovoked seizures are considered as epilepsy. Single seizure episode is not considered as epilepsy. Series of seizures occurring in a single day are usually considered as single seizure episode.

ACUTE SYMPTOMATIC SEIZURE

Acute symptomatic seizures are seizures that occur at the time of a systemic insult or in close temporal association with a documented brain insult. It is otherwise called as situation related seizures, reactive seizures or provoked seizures.

THE NEURO PHYSIOLOGY OF EPILEPSY

EPILEPTOGENESIS

Epileptogenesis refers to the transformation of a normal neuronal network into one that is chronically hyperexcitable. There is often a delay of months to years between the initial CNS injury and the first seizure. The injury appears to initiate a process that gradually lowers the seizure threshold in the affected region until a spontaneous seizure occurs.

BASIC MECHANISMS OF EPILEPTOGENESIS[6]

Paroxysmal Depolarization Shift

In epileptic conditions, the membrane potential of cortical and deep seated neurons changes enormously to an extent that far exceeds the usual physiological changes occurring with neuronal excitation.

A large paroxysmal depolarization shift (PDS) is capable of changing the resting membrane potential of –85mV to +30Mv. This enormous shift is accompanied by massive bursts of rapid neuronal spikes. PDS originating from a wide cortical regions are associated with spike discharges recorded from scalp EEG.

Neurotransmitters

Excitatory neurotransmitters are naturally involved in epileptogenesis, initiation and propagation of seizures. Glutamate, aspartate and especially N-methyl-D- aspartate (NMDA) have been recognized as the most active neuro excitatory transmitter. Gamma amino butyric acid (GABA) is considered the most powerful inhibitor of epileptic mechanisms. Naturally, failure of GABA may strongly contribute to epileptogenesis, initiation and propagation of seizures.

Ions are of great importance. The sodium pump has been thought to be of special significance in epileptogenesis, neuronal excitability and hence epileptogenicity is governed by the interaction of voltage and ligand gated ion channels.

SEIZURE INITIATION AND PROPAGATION

With increasing influx of afferent signals, massive depolarization and hypersynchronization, a negative direct current shift starts heralding an epileptic event. The transition may also be related to a breakdown of local inhibitory mechanisms.

Intracortical propagation of epileptic activity may occur from dendrite to dendrite or from soma to soma. The most important mechanism is synaptic propagation along conducting pathways.

SECONDARY EPILEPTOGENESIS

Secondary epileptogenic foci may result from the spread of epileptic activity. A secondary focus was found in the region of callosal terminations of the neurons involved in the primary focus.

ANIMAL MODELS

An experimental animal model for focal epilepsies has been done using penicillin, maximal electroshock, phenylenetetrazol, strychnine, tetradotoxin, pilocarpine and nicotine.

KINDLING

Kindling denotes repeated subthreshold electrical stimulation of various cerebral regions especially in limbic areas. The kindling technique aims at the gradual escalation of epileptic activity culminating in spontaneous seizures. The kindling effect is absent in the human.

ENDOGENOUS FACTORS

There are various underlying endogenous factors that influence the threshold for having a seizure. Some of the factors are clearly genetic. It has been shown that a family history of epilepsy will influence the likelihood of seizures occurring in otherwise normal individuals.

EPILEPTOGENIC FACTORS

There are various conditions that have an extremely high likelihood of resulting in a chronic seizure disorder. Examples are head trauma, stroke, CNS infections, and abnormalities of CNS development. These factors transform a normal neural network into one that is epileptogenic.

PRECIPITATING FACTORS

These factors induce or provoke a seizure in patients with epilepsy. Similarly, precipitating factors are responsible for causing the single seizure in someone without epilepsy. Examples are sleep deprivation, psychological

or physical stress, fever, menstruation, exposure to drugs or toxic substances, metabolic disturbances.

CLASSIFICATION OF SEIZURES

Determining the type of seizure that has occurred is essential for focusing the diagnostic approach on particular etiologies, selecting the appropriate therapy and providing vital information regarding prognosis. In 1981,the International League Against Epilepsy (ILEA) published a modified version of international classification of epileptic seizures[1] that has continued to be a useful classification system.

SEIZURE CLASSIFICATION BY ILAE

I. PARTIAL SEIZURES:

A. Simple partial seizures

1.With motor signs:

a) focal motor without march

b) Focal motor with march (Jacksonian)

c) Versive

d) Postural

e) Phonatory (Vocalization or arrest of speech)

2.With sensory symptoms:

a) somatosensory

b) Visual

c) Auditory

d) Olfactory

e) Gustatory

f) Vertiginous

***3.With autonomic symptoms or signs*:**

- Epigastric sensation
- Pallor
- Sweating
- Pilo erection
- Pupillary dilatation

4. With psychic symptoms: - (more commonly experiences as Complex partial seizures)

a) Dysphasic

b) Dysmnesic

c) Cognitive (dreamy state, distortions of time sense)

d) Affective (fear, anger)

e) Illusions (e.g. macropsia)

f) Structured hallucinations (e.g. music, scenes)

B. Complex partial seizures

1.simple partial onset

a) With simple partial features followed by impaired consciousness
b) With automatisms

2. With impairment of consciousness at onset: -

a) With impairment of consciousness only
b) With automatisms.

B. Partial seizures evolving to secondary generalized seizures:

1.simple partial seizures evolving to generalized seizures

2.complex partial seizures evolving to generalized seizures.

II. GENERALISED SEIZURES

A. Absence seizures

1. Typical absences
2. Atypical absences

B. Myoclonic seizures (myoclonic jerks, single or multiple)

C. Clonic seizures

D. Tonic seizures

E. Tonic clonic seizures

F. Atonic seizures

3.UNCLASSIFIED EPILEPTIC SEIZURES

4.ADDENDUM (With respect to occurrence of seizure (cyclic, fortuitous) or precipitation by triggering events.

PARTIAL SEIZURES

Partial seizures occur within discrete regions of brain. If consciousness is fully preserved during the seizure, the seizure is called simple partial seizure. If consciousness is impaired, the seizure is termed as complex partial seizures.

Simple Partial Seizures

Simple partial seizures cause motor, sensory, autonomic, psychic symptoms without obvious alteration in consciousness. The EEG recorded with scalp electrodes during seizure may show abnormal discharges over appropriate area of cerebral cortex.

Complex Partial Seizures

Complex partial seizures are characterized by focal seizure activity accompanied by a transient impairment of the patient's ability to maintain normal contact with the environment. The seizures frequently begin with an aura (i.e., a simple partial seizure) that is stereotypic for the patient. The start of the ictal phase is often a sudden behavioral arrest or motionless stare.

The behavioral arrest is usually accompanied by automatisms such as chewing, lip smacking, swallowing or picking movements of the hand. There will be post ictal confusion. The patient is not aware and cannot recollect the ictal events.

Partial Seizures with secondary Generalization

Partial seizures can spread to involve both hemispheres and produce a generalized seizure, usually of the tonic clonic variety.

GENERALIZED SEIZURES

(arise from both cerebral hemispheres simultaneously)

Absence Seizures

Absence seizures are characterized by sudden, brief lapses of consciousness without loss of postural control. The seizure typically lasts for only a few seconds and there is no post ictal confusion. Absence seizures usually begin in childhood. The EEG hallmark is generalized, symmetric, 3 HZ spike and wave discharge that begins and ends suddenly superimposed on a normal EEG background.

Generalized Tonic Clonic Seizures (GTCS)

They are main seizure type in 10% of all persons with epilepsy. The seizure usually begins abruptly, sometimes with premonitory symptoms. In the initial phase, there will be tonic contraction of muscles throughout the

body leading to temporary arrest of respiration, pooling of secretions in the oropharynx, cyanosis. Contraction of jaw muscle may cause tongue bite. After 10-20 seconds, the tonic phase of seizure typically evolves into clonic phase, produced by superimposition of periods of muscle relaxation, which usually lasts about 1 minute.

The post ictal phase is characterized by unresponsiveness, muscular flaccidity, and bowel and bladder incontinence. Post ictal unresponsiveness and confusion will last for minutes to hours.

Atonic Seizures

Atonic seizures are characterized by sudden loss of postural muscle tone lasting 1-2 seconds. Consciousness is briefly impaired, but there is no post ictal confusion.

Myoclonic Seizures

In myoclonic seizure, there is a sudden brief muscle contraction that may involve one part of the body or the entire body. There may be a single jerk or asynchronous jerks involving multiple body parts. They are the predominant feature of juvenile myoclonic epilepsy.

EPILEPSY IN ADULTS

Epilepsy in adults is otherwise known as “late onset epilepsy”. It is defined as epilepsy that starts after 25 years of age[17]. Around 25% of the patients with epilepsy had their first seizure after 25 years of age.

Epilepsy in adult life is often symptomatic and frequently has neurological or metabolic disorder, unlike children and adolescents with epilepsy who will present with typical epileptic syndromes, which are idiopathic.

Not all seizures occurring during adult life are due to epilepsy. Many are acute symptomatic seizures, which should be recognized to avoid inappropriate long-term antiepileptic drug treatment. Acute symptomatic seizure can complicate any acute encephalopathy caused by drugs or metabolic disturbances.

Most of the patients presenting with epilepsy in adult life will have a form of partial epilepsy. So, structural brain abnormalities should be carefully ruled out in adults with epilepsy.

ETIOLOGY OF SEIZURES IN ADULTS[1]

1. Cerebrovascular disease

2. Space occupying lesions

a. Brain tumors

b. Neurocysticercosis

c. Tuberculoma

d. Lymphoma

e. Toxoplasmosis

f. Cerebral abscess

g. Hydatid cyst

3. CNS infections

4. Posttraumatic seizures

5. Alzheimer's disease and other degenerative brain disease.

6. Risk factors for embolic stroke

(i) Ischemic heart disease

(ii) Atrial fibrillation

(iii) Cardiomyopathies

7.Acute symptomatic seizures

(i) ***Head injury*** –

Subdural hematoma

Extradural hematoma

Subarachnoid hemorrhage

Intracerebral hemorrhage

(ii) ***Stroke***

Ischemic cerebral infarct

Intracerebral hemorrhage

(iii) ***CNS infections*** -

Meningitis

Encephalitis

(iv) ***Metabolic disturbances***-

Hypoglycemia

Hyperglycemia

Hypo, hypernatremia

Renal failure

Hepatic encephalopathy

Hypercalcemia

Hypomagnesemia

(v) ***Endocrinological*** –

Hyperparathyroidism

Thyrotoxicosis

Hashimoto's encephalopathy

(vi) Drug toxicity and withdrawal

Alcohol

Cocaine, Amphetamine

Antidepressant overdosage

Antipsychotic overdosage

Benzodiazepine or barbiturate withdrawal

β Lactam antibiotics

Isoniazid

Lithium

Theophylline

(vii) Eclampsia

8. **Other rare causes**

Vasculitis (like SLE, PAN etc)

Connective tissue disorders

Sarcoidosis

9.**Idiopathic**

EVALUATION OF THE ADULT PATIENTS WITH EPILEPSY[4]

When a patient presents shortly after a seizure, the first priorities are attention to vital signs, respiratory and cardiovascular support and treatment of seizures. Life threatening conditions such as metabolic insults like hypoglycemia, drug toxicity or CNS infection should be identified and treated accordingly.

When the patient is not acutely ill, the evaluation should focus on the following

(i) Whether the reported episode was a true seizure or a paroxysmal event other than a seizure.

(ii) To identify the cause of seizure by identifying risk factors and precipitating factors.

(iii) To decide whether anticonvulsant therapy is required in addition to treatment of an underlying illness.

If the patient had prior history of epilepsy, then evaluation should focus on

(i) Identification of the underlying cause and precipitating factors

(ii) Determination of adequacy of dose of anticonvulsants taken by the patient

(iii) Assessment of the patient's compliance and adherence to therapy.

HISTORY

Epilepsy is essentially a historical diagnosis. So, the patient and the family members should be questioned carefully about the seizure event to determine whether the event was truly a seizure. Many paroxysmal events can mimic a seizure even to an educated person, unless a doctor witnesses the episode.

PAROXYSMAL EVENTS THAT CAN MIMIC A SEIZURE

(1) **Syncope**

Vasovagal syncope

Cardiac syncope (Stokes Adams Attacks, Brady and tachyarrythmias)

Orthostatic syncope

(2) Psychological disorders

Psychological seizure (Pseudo seizures)

Hyperventilation anxiety attacks

Panic disorders

Depersonalization

Psychogenic fugue

(3) **Metabolic disorders**

Alcoholic blackouts

Delirium tremens

Tetanus

Hypoglycemia

Porphyria

(4) **Migraine** –

Confusional migraine

Basilar migraine

(5) **TIA**

Basilar artery TIA

(6) **Sleep disorders**

Narcolepsy/cataplexy

Benign sleep myoclonus

(7) **Movement disorders**

Tics

Non epileptic myoclonus

Paroxysmal choreoathetosis

Paroxysmal dystonia

(8) Miscellaneous

Idiopathic drop attacks of the elderly

Transient global amnesia

Benign paroxysmal vertigo

Night terrors

DIFFERENTIATING PSEUDO SEIZURE FROM EPILEPTIC SEIZURE[8]

PSEUDO SEIZURE	EPILEPTIC SEIZURE
Preceding Ictus	
- Absence of explanatory disease	Frequent evidence of neurological disease
- Anxiety aura – Palpitation, Choking etc	Wide range of epileptic auras
- Seizures may be induced by suggestions	Rarely induced except for reflex seizures
During Ictus	
- Inconsistencies in clinical presentation	The presentation fit specific seizure types
- Only occur when others are present	Often occurs without witnesses or during sleep
- Gradual onset, prolonged duration(> 2 min)	Abrupt onset, short duration (< 2 min)
- Whole Body rigidity is rare	Tonic rigidity of whole body occurs
- Asymmetrical, out of phase movements, pelvic thrusts and hyperarching	Decrescendo symmetric clonic activity in GTCS
- Rare incontinence, tongue bite, self injury	Tongue bite, incontinence if generalized
- Avoids noxious stimuli or eye opening	Cannot avoid noxious stimuli
After Ictus	
- No postictal confusion,	Typical Postictal delirium
- No increase in prolactin	Increased serum prolactin
- Normal post ictal EEG	Postictal slowing in EEG
- Subsequent recall of events during ictus	No recall of ictal events.

CLINICAL EXAMINATION

Careful physical examination should be done to search for signs of infection, systemic illness like chronic liver or renal disease. Signs of head injury and alcohol or illicit drug usage should be searched. Detailed cardiovascular examination should be done to rule out a cardiac problem that predisposes to cerebrovascular disease. Complete neurological examination should be done with particular emphasis on eliciting signs of cerebral hemispheric disease and signs of meningeal irritation.

LABORATORY STUDIES

Routine blood studies are done to identify a metabolic abnormality. Blood sugar, creatinine, calcium, magnesium, electrolytes, liver function tests are done in the initial assessment. A screen for toxins in blood and urine should also be done from patients in appropriate risk groups. CSF analysis should also be done, if there is suspicion of meningitis or encephalitis.

NEUROIMAGING IN ADULT PATIENTS WITH EPILEPSY

All adult patients with seizures should undergo brain imaging with either CT scan or MRI to rule out a structural abnormality. The disadvantage of CT scan is that it can identify only macroscopic pathology in the brain like cerebral infarct or large destructive lesion. Small lesions like low-grade glioma, lacunar infarct may be missed in CT scan.

MRI brain is the most sensitive investigation to evaluate an adult patient with epilepsy. In some cases MRI will identify lesions such as tumors, vascular malformations or other pathologies that need immediate therapy. The use of new MRI methods like, Fluid-attenuation inversion recovery (FLAIR), has increased the sensitivity for detection of abnormalities. MRI will identify patients and point to the need for chronic anticonvulsant therapy or possible surgical correction. The disadvantage is that it is costly and may not be available at all centres.

ROLE OF EEG IN ADULT PATIENTS WITH EPILEPSY

One of the major uses of EEG is in the investigation of patients with suspected epilepsy. In this regard, the presence in the EEG of interictal spike discharges or sharp wave is often held to be suggestive of an epileptic disturbances. EEG also provides a non-invasive means of localizing structural abnormalities, such as brain tumors. Moreover, it is sometimes inaccurate. So EEG is a complement, rather than alternative to newer procedures like CT scan and MRI.

EEG can identify a focal or lateralized epileptic source in adult patients with epilepsy. So it is an useful tool to identify the focal seizure activity.

Epileptiform Activity

Epileptiform activity is defined as abnormal paroxysmal activity consisting of spikes or sharp waves resembling those found in many patients with epilepsy.

A spike is defined arbitrarily as a potential having sharp outline and duration of 20- 70 millisecond, whereas a sharp wave has a duration of 70-200 millisecond.

Focal epileptiform spike discharges arise from a localized cerebral region. Slowly progressive lesions are more likely to be associated with such activity than are rapidly progressive ones and frontal and temporal lobes are more epileptogenic.

Periodic Lateralized Epileptiform Discharges (PLED)

Repetitive epileptiform discharges sometimes occur periodically as a lateralized phenomenon. They typically are seen in patients with hemispheric lesions caused by cerebral infarction, hemorrhage or tumors. PLEDs are more likely when there are associated metabolic derangement, especially hyperglycemia and fever. During the acute stages of illness patients with PLED are usually obtunded and commonly have seizures and a focal neurological deficit. These epileptiform activities can be induced by hyperventilation or photic stimulation.

AIMS OF THE STUDY

1. To evaluate the common etiological and risk factors for the development of epilepsy in adults.
2. To find out the incidence of abnormal CT scan imaging in adult patients with epilepsy.
3. To find out the role of abnormal metabolic events in the development of seizures in adults.
4. To study the role of EEG in the diagnosis of epilepsy in adults.

MATERIALS AND METHODS

Epilepsy is primarily a historical diagnosis. The initial assessment and approach to management based solely on the clinical history, especially on an accurate description of event in question. Laboratory studies are often normal. The first goal is to determine whether the event was truly a seizure.

Information should be obtained from the patient when possible, as well as from family members who have observed typical attacks. Complete physical and neurological examination is mandatory. Routine Blood studies, EEG, Brain imaging will aid in the diagnosis of seizures.

SELECTION OF PATIENTS

Inclusion Criteria

In this study, the patients who presented with seizures after 25 years of age and of both sexes were included.

Exclusion Criteria

The patients with the following characteristics were excluded from study.

- History suggestive of seizure before 25 years of age
- History suggestive of a diagnosis of pseudoseizure or a paroxysmal event other than seizure.
- H/O Neonatal/ Febrile seizure
- Cerebral palsy
- Mental retardation, speech disorder or Learning disorder since childhood.
- Presence of Neurological abnormalities since childhood (Like Hemiparesis, Cranial nerve deficit, dystonia, movement disorder. etc.)

No. of Cases Studied: 42

Study Period: - December 2004 – June 2006.

STUDY METHODS

Patients who presented with seizures after 25 years of age and of both sexes, who were admitted in medical wards and in the neurology ward of Thanjavur Medical College Hospital from December 2004 to June 2006 were taken up for this study.

Patients were excluded from the study if the history suggested a diagnosis of pseudoseizure or a paroxysmal event other than seizure, or seizure onset before 25 years of age. Patients were excluded from the study if there was a history of neonatal or febrile seizures. Patients with mental retardation and or neurological abnormalities since childhood were excluded from the study.

The selected patients were subjected into the following examination,

1. Detailed History taking.
2. Clinical Examination.
3. Laboratory studies.
4. CT Brain Plain (Contrast if necessary).
5. EEG

I. History Taking

History was taken carefully both from the patients and from the family members who observed the episode. Questions were focused on the symptoms before, during, and after the episode in order to discriminate a seizure from other paroxysmal events. The following details were collected from the history.

1. Aura
2. Subsequent evolution of seizure (tonic, clonic movements, cry, tongue bite, body injury, involuntary micturition)
3. Post ictal manifestations (Confusion, Amnesia, Todd's paresis)
4. Date and circumstance of first attack
5. Age of onset of seizure
6. Average frequency of attack
7. Longest seizure free interval
8. Precipitating factors (Sleep deprivation, systemic disease, acute infection, electrolyte or metabolic insult, drug)
9. Details of AED. (Anti Epileptic Drugs)
10. History was also focused on the risk factors and predisposing events like,
    - Family History of seizure
    - Previous Head injury
    - Previous stroke or TIA

- CNS infection
- Dementia
- Alcoholism
- Risk factors for Embolic stroke [HT/DM/ CAHD/A.F]
- Drug intake (Illicit drugs, Antipsychotic, Antidepressant)

II. CLINICAL EXAMINATION

General physical examination was done to search for signs of infection, systemic illness, chronic liver or renal disease, signs of head trauma.

Blood pressure recording and examination of all peripheral pulses were done to rule out systemic hypertension and atrial fibrillation. Auscultation of heart and carotid artery was done to search for cardiac murmurs and carotid artery bruit, which may be a predisposing factor for stroke.

Mental status examination and complete neurological examination of all patients were done with particular emphasis on eliciting signs of cerebral hemispheric disease.

3. LABORATORY INVESTIGATIONS

The following Laboratory study was done to all the patients.

-	Blood sugar	-	Serum Calcium
-	Blood urea	-	Liver function tests
-	Serum creatinine	-	X Ray Chest PA view
-	Serum Electrolytes	-	ECG

4. **EEG :** EEG was done to all the patients in the study during postictal Period.

5. **BRAIN IMAGING**:- CT Scan imaging of Brain was done for all the patients in the study. Contrast CT Brain was done for selected patients if necessary. (eg. If a hypodense lesion suggestive of SOL was found in the plain CT.)

OBSERVATION AND RESULTS

All observations made are recorded in various tables. Totally, 42 cases of seizures in adults aged more than 25 years were studied with blood biochemistry, CT Brain and EEG.

AGE INCIDENCE

The minimum age noted was 26 years, the maximum - 75 years of age. Major incidence was noted in the 25-40 years of age. (55%). The minimum incidence was noted in the 40-60 years of age (19%).

TABLE – I

AGE INCIDENCE

AGE IN YEARS	NO. OF CASES	PERCENTAGE
25-40	23	55%
40-60	8	19%
60-80	11	26%

SEX INCIDENCE

Male preponderance was noted. Male to female ratio was 3:1.

TABLE – II

SEX INCIDENCE

SEX	No. of Cases	Percentage
Male	31	74%
Female	11	26%

TABLE – III

AGE AND SEX INCIDENCE

Etiology	Total No. of Cases	Male	Female	Age in Years		
				25-40	40-60	60-80
Cerebrovascular Disease	8	6	2	1	3	4
Space occupying lesions	4	4	0	3	0	1
Head injury	3	2	1	2	1	0
CNS infection	1	0	1	1	0	0
Risk factors for embolic stroke	3	3	0	1	0	2
Nonketotic Hyperglycemia	3	1	2	0	1	2
Alcohol withdrawal	1	1	0	1	0	0
Renal disorder	2	2	0	1	1	0
Idiopathic	17	12	5	13	4	0

TYPE OF SEIZURE

GTCS (Generalized Tonic Clonic Seizure) was the most common seizure type observed, followed by simple motor partial seizures and partial seizures with secondary generalization..

TABLE – IV

TYPE OF SEIZURE

SEIZURE TYPE	No. of Cases	Percentage
GTCS	34	81%
Simple partial motor	6	14%
Complex partial	0	0
Partial Seizures with Secondary generalization	2	5%
Myoclonic	0	0
Absence	0	0

ETIOLOGY OF SEIZURES IN ADULTS

Most of the seizures in adults (60%) were symptomatic. Only 40% of seizures were idiopathic. Cerebrovascular disease was the most common cause of seizures in the symptomatic group. Other causes were post traumatic seizures, space occupying lesions, alcoholism, metabolic disorders.

TABLE – V

ETIOLOGY OF SEIZURES IN ADULTS

Etiology	No. of. Cases	Percentage
Cerebro Vascular Disease	8	19%
Space occupying lesions	4	10%
Head injury	3	7%
CNS infection	1	2%
Nonketotic hyperglycemia	3	7%
Risk factor for embolic stroke	3	7%
Alcohol withdrawal	1	2%
Renal disorder	2	5%
Idiopathic	17	41%

SEIZURES DUE TO METABOLIC PROBLEM

About 10% cases had seizures due to metabolic disorder. Nonketotic hyperglycemia was the most common metabolic insult causing seizure.

TABLE – VI

METABOLIC SEIZURES IN ADULTS

Metabolic Disorder	No. of Cases	Percentage
Nonketotic hyperglycemia	3	60%
Uremic encephalopathy	1	20%
Acute Glomerulonephritis	1	20%

ACUTE SYMPTOMATIC SEIZURES

About 17% cases had acute symptomatic seizures. Again, nonketotic hyperglycemia was the most common cause of acute symptomatic seizure.

TABLE – VII

ACUTE SYMPTOMATIC SEIZURES

Causes	No. of Cases	Percentage
Nonketotic hyperglycemia	3	44%
Acute Glomerulonephritis	1	14%
Alcohol withdrawal	1	14%
Uremic encephalopathy	1	14%
Bacterial Meningitis	1	14%

PATIENTS WITH ABNORMAL CT BRAIN

13 patients had abnormal CT scan imaging of brain. Ischemic cerebral infarct was the most common finding observed, followed by space occupying lesions.

TABLE – VIII

PATIENTS WITH ABNORMAL CT BRAIN

CT Scan Findings	No. of Cases	Percentage
Ischemic infarct	8	60%
Bilateral Multiple Neurocysticercosis	1	8%
Calcified Granuloma	1	8%
Brain Tumour	1	8%
Single nodular enhancing lesion	1	8%
Gliosis due to old ICH	1	8%

PATIENTS WITH ABNORMAL EEG

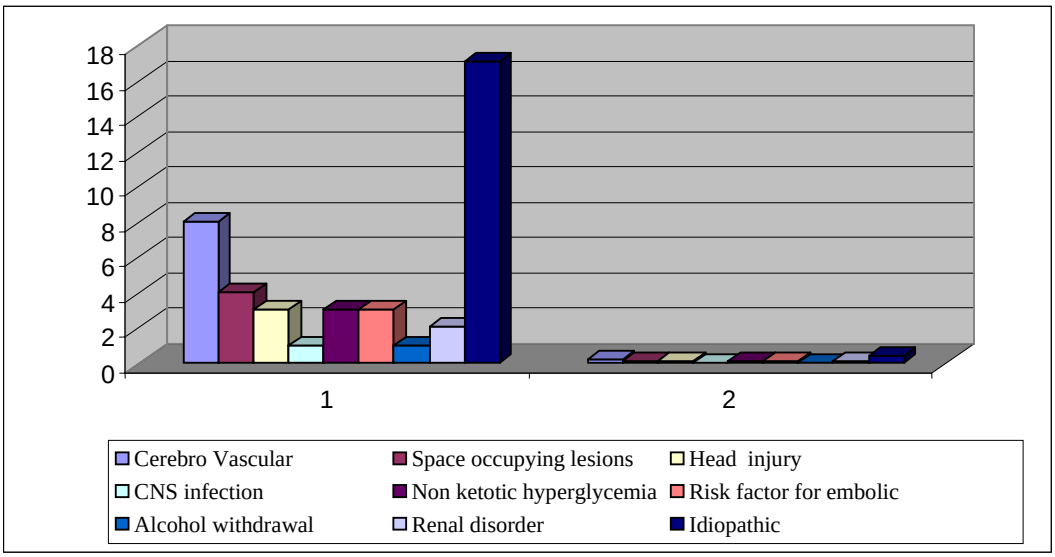
19% of patients had abnormal epileptiform activity in the interictal EEG.

TABLE – IX

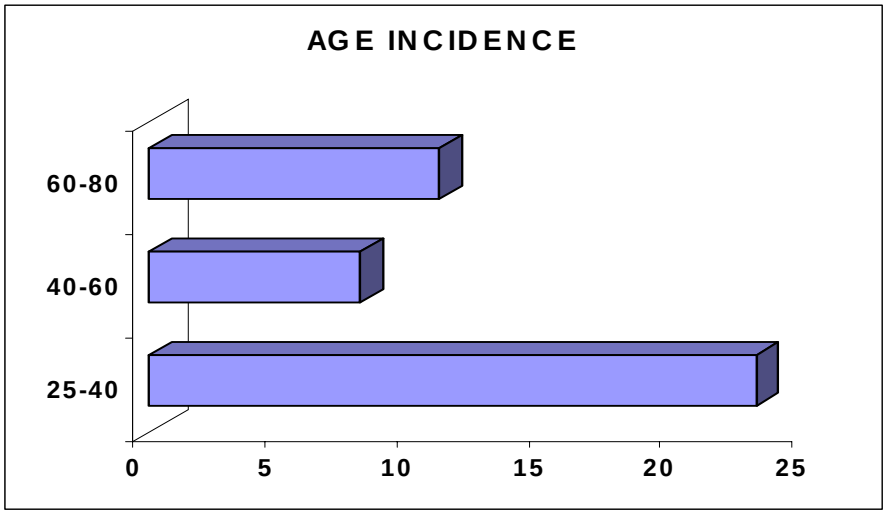
PATIENTS WITH ABNORMAL EEG

EEG Findings	No. of Cases	Percentage
Normal	34	81%
Lateralizing Epileptiform activity	8	19%

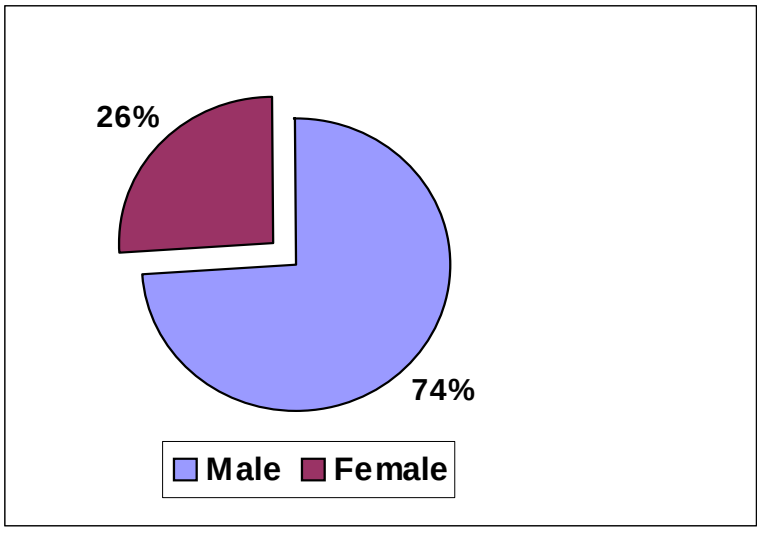
ETIOLOGY OF SEIZURES IN ADULTS



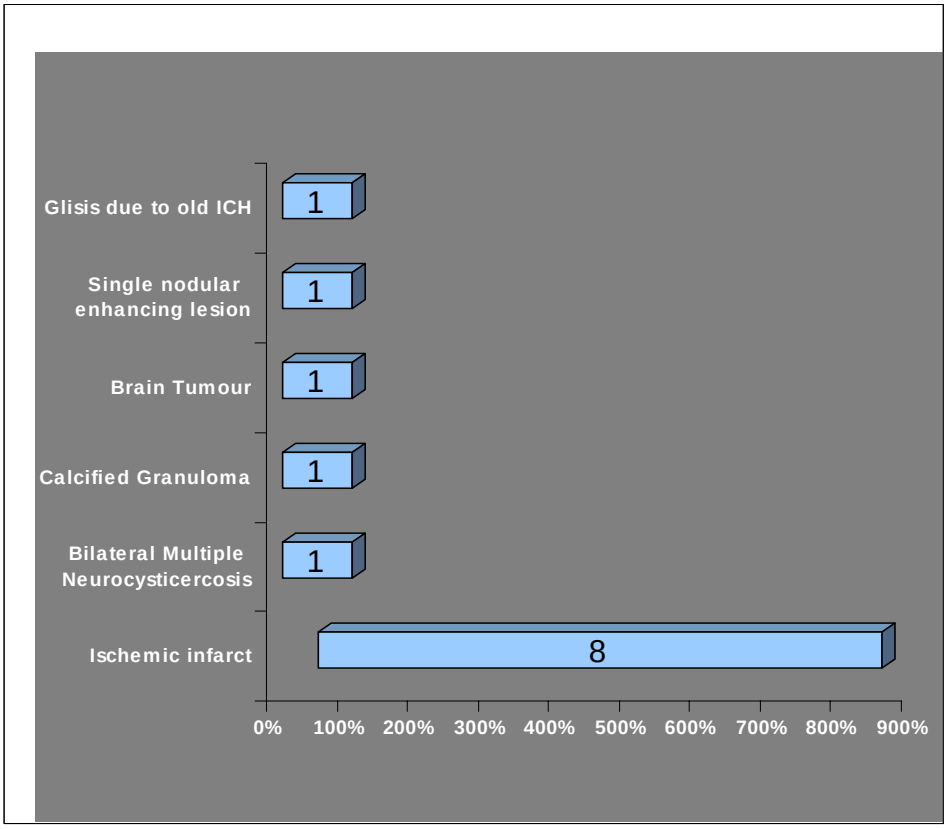
AGE INCIDENCE



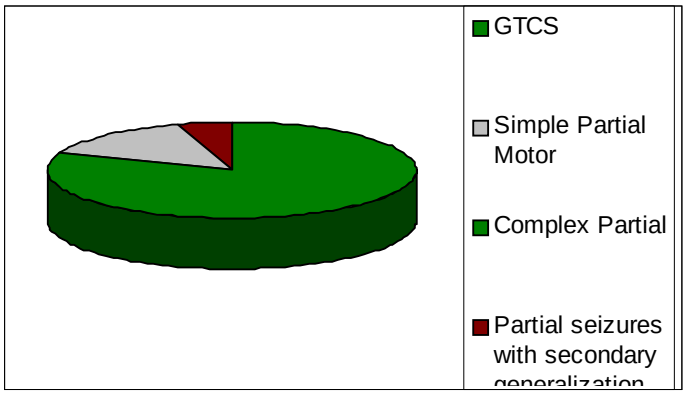
SEX INCIDENCE



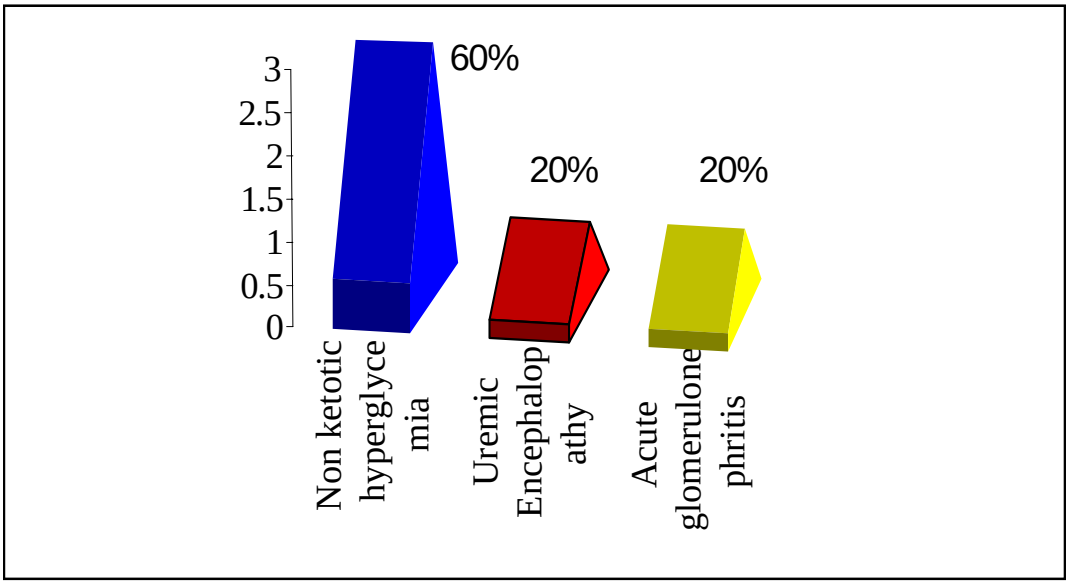
PATIENTS WITH ABNORMAL CT BRAIN



TYPE OF SEIZURES IN THIS STUDY



METABOLIC SEIZURES IN THIS STUDY



DISCUSSION

Epilepsy may develop in adults for a number of reasons. Epilepsies in children and adolescents are characterized by a high probability of generalized spike and wave in the EEG, and patients will be neurologically normal and do not require further investigation.

Most of the patients presenting with epilepsy in adult life often have underlying neurological disorder or metabolic insult, which should be identified carefully and treated accordingly. About 50% of patients with adult onset epilepsy have no etiology that can be determined by the investigatory means currently available.

In this study of ``**Epilepsy in Adults``,** out of 42 cases, major proportion of cases (25 cases) had identifiable neurological, metabolic or other factors that caused the seizure. Out of these 25 cases, majority of patients had cerebrovascular disorders (8 cases, 32%), mostly of ischemic cerebral infarct. Other causes noted in the study were 3 cases (12%) of post traumatic seizures, 1 case of (4%) bacterial meningitis, 3 cases of (12%) hyperglycemic fits, 1 case of (4%) alcohol withdrawal seizure and 2 cases of renal failure.

3 patients (12%) had risk factors for embolic stroke like ischemic heart disease, rheumatic heart disease, hypertension but without previous history of stroke. In about 17 cases (40%), no etiology could be determined and were considered as idiopathic epilepsy.

AGE INCIDENCE

In this study, most of the patients (55%) with seizures were young adults in the range of 25-40 years. In this study, idiopathic epilepsy was most commonly found (53%) in these young adults. 67% of post traumatic seizures occurred in this age group. Among the patients with space occupying lesions, 75% of patients belonged to this group.

Most patients (87.5%) with seizures due to cerebrovascular disorders were more than 40 years of age, and the incidence increased in patients with age more than 60. All the elderly patients aged more than 60 in the study had some identifiable cause for their seizure. Cerebrovascular disease was found to be the commonest cause of epilepsy in the elderly. Idiopathic epilepsy was not found in elderly patients.

A British general practice survey reported that almost 25% of all newly identified seizures occurred in persons aged 60 and over. In studies from Asia and Africa, the peak incidence of epilepsy occurred in young adults[1].

SEX INCIDENCE

Most of the patients in this study were males. The male to female ratio was 3:1. Various authors like J.Engel and T.A.Pedley also showed male preponderance. The consistency of male to female difference across studies suggests that males are at higher risk than females for development of seizures[1].

SEIZURE TYPE

In this study, generalized tonic clonic seizure was the commonest (81%) seizure type observed. The remaining cases were of partial seizure types. Of these, 6 cases were simple motor partial seizures and other 2 cases were partial seizure with secondary generalization. Complex partial seizure, myoclonic seizure or absence seizures were not detected in this study.

Out of 8 patients with partial seizures, 5 patients had lesions in the CT Brain. 4 patients had cerebral infarct and 1 patient had single nodular enhancing lesion in the CT Brain. 3 other patients had partial motor seizures due to uncontrolled diabetes mellitus. Onset of partial seizure during adult life is most commonly associated with the identification of an underlying neurological abnormality. So, structural brain abnormalities should be ruled out in patients presenting with partial seizures[4].

ETIOLOGICAL AND RISK FACTORS

CEREBROVASCULAR DISEASE

In this study, cerebrovascular disease was the major etiological factor (19%) that caused unprovoked seizures in adults. Out of 8 patients in this group, 7 patients had cerebral infarct and 1 patient had gliosis in the brain parenchyma due to old cerebral hemorrhage. Most patients were more than 40 years of age. The incidence of cerebrovascular disease causing seizure increased in patients aged more than 60. A study conducted by Pantificia University Hospital, Brazil reported that stroke is the most common etiology (18%) in patients with adult onset epilepsy.

In our study, out of 8 patients with cerebrovascular disease, 4 cases had partial seizure type. 2 cases were simple motor partial seizures and other 2 cases were partial seizures with secondary generalization. The remaining cases were generalized tonic clonic Seizure. Various studies showed that partial seizure is the most commonly observed seizure type in patients with cerebrovasular disease[16].

In our study, cerebrovascular disease was the most common cause of seizure in the elderly patients aged more than 60 years. This observation is also favoured by the statement by the author T.A. Pedley that ``In developing countries cerebrovascular disease is the most common cause of seizures in the elderly``.

All these 8 patients had risk factors like ischemic heart disease, hypertension, diabetes mellitus, smoking or rheumatic heart disease with atrial fibrillation. Most of the patients (60%) had their seizure onset along with the onset of stroke, i.e. seizures presented immediately or in the first 48 hours after stroke. In a study conducted by stroke unit, Department of Neurology, Ghent University Hospital, it was found that seizures occurred within 48 hours of stroke and most of the patients developed recurrent seizure within 2 years of stroke.

In our study, 4 out of 8 patients had neurological deficit. The presence of neurological deficit carries a high risk of development and recurrence of seizure. The oxford community stroke study[16] found that 2.1% of patients had a seizure within 24 hours of stroke and 7.1% had seizures subsequently. The one-year cumulative risk of poststroke seizure was 4.1% after cerebral infarction, 18.2% after primary intracerebral hemorrhage and 27.8% after subarachnoid hemorrhage.

SPACE OCCUPYING LESIONS

In this study, 4 patients (10%), were found to have space occupying lesions in the brain. One patient had non enhancing brain tumour, suspicious of glioma. One patient had multiple bilateral neurocysticercosis which appeared in the CT Brain as multiple ring enhancing lesions. One patient had single nodular

enhancing lesion in the brain, suspicious of tuberculoma, another patient had a calcified cerebral granuloma. Biopsy was not done in this study from the lesion to confirm the diagnosis. In various studies, it has been shown that average incidence of space occupying lesions in adult onset epilepsy is 12%.

Interestingly, single small contrast enhancing lesion in CT Brain appears to be particular to Indian subcontinent, from where most of the published work originated. In India presence of such lesions has been noted from all regions of country. Tuberculoma, neurocysticercosis, glioma, microabscess, vascular malformation, cavernous angioma, sarcoidosis, focal encephalitis are the differential diagnosis for such lesions. Majority of patients will present with simple partial motor seizures[5].

In endemic regions, the presence of adult onset seizures in an otherwise healthy middle aged individual is highly suggestive of neurocysticercosis[5]. Most of the patients had either partial or generalized seizures. Most of the patients will present with multiple ring-enhancing lesions in the CT Brain.

Brain tumors remain a relatively rare cause of epilepsy[16]. In one series tumors were detected in 16% patients who developed epilepsy over the age of 20. The siting of the tumour also appears to influence the likelihood of a presentation of epilepsy.

Tumours located in the parietal region has high tendency to produce seizures. Among the brain tumours, oligodendroglioma has more tendency (92%) to produce seizure followed by astrocytoma (70%).

POST TRAUMATIC SEIZURES

Head injury increases the risk for later unprovoked seizure, with greater risk occurring among survivors of severe head injury. In our study, 3 patients had posttraumatic seizures, 1 patient had mild head injury and 2 other patients had severe head injury with loss of consciousness of more than 24 hours. 2 patients with severe head injury had their seizure onset within 1 month of head injury. 1 patient with mild head injury had seizure onset after 1 year of head injury.

These observations are supported by a study of Vietnam veterans who survived head injury. It showed that risk for remote symptomatic seizure increased 580 fold during the first 12 months after the injury and 25 fold after 10 years. The increased risk for subsequent seizure was related to severity of head injury. The risk of unprovoked seizure was 30 fold after severe injury and 4 fold after moderate injury.

CNS INFECTION

Infection of CNS like encephalitis and meningitis are associated with an increased risk for subsequent unprovoked seizure. In our study, no patients had previous history of CNS infection, but, 1 patient had acute symptomatic seizure due to bacterial meningitis. The risk of unprovoked seizure is higher with encephalitis than meningitis.

RISK FACTORS FOR EMBOLIC STROKE

Risk factors for embolic stroke in patients with no previous history of stroke are associated with increased risk of seizures[22]. The risk factors are systemic hypertension, ischemic heart disease, rheumatic heart disease, atrial fibrillation and cardiomyopathy. A case control study of acute cerebrovascular accident by Shinton et. al., reported that prevalence of epilepsy preceding stroke was 4.55%, compared with 0.6% among controls. This led to the fact that risk factors for stroke are also risk factors for unprovoked seizure.

A population based case control study conducted in Minnesota revealed that presence of a risk factor for embolic stroke increased the risk of both generalized and partial seizures two fold. In our study 3 patients had risk factors for embolic stroke without prior history of stroke. One patient had rheumatic heart disease with atrial fibrillation and other 2 patients had risk factors like hypertension and ischemic Heart disease.

ALCOHOLISM

Alcohol intake appears to be associated with seizure occurrence[1]. A case control study in Harlem in NewYork found a dose response between alcohol consumption and risk for seizure. A case control study from Nigeria also associated alcohol consumption with seizure. In our study, 14 patients (33%) were alcoholic. 1 patient had GTCS directly related to alcohol withdrawal.

In those with alcoholism who have seizures, alcohol withdrawal is the most common cause of seizure. 3 clinical series were conducted in alcohol abusing patients who presented with acute seizures. 80% of seizures are due to alcohol withdrawal and the remaining due to head injury, hypoglycemia, stroke, and abuse of other drugs. Most common seizure type observed was GTCS.

ACUTE SYMPTOMATIC SEIZURES

Acute symptomatic seizures typically occur within first week of an insult known to predispose to seizures and are not regarded as epilepsy. Though they are not diagnosed as epilepsy, these cases are also included in our study because of the following reasons.

1. They are the most frequently occurring class of seizures in adults and still account for a substantial proportion of all newly occurring seizures.

2. Studies suggest that such seizures increase the risk for later epilepsy at least 3 fold, because their occurrence is a marker for severity of brain injury.

In our study 7 cases were of acute symptomatic seizures. 3 cases were due to hyperglycemia in patients with uncontrolled diabetes mellitus, 2 cases were due to renal causes - 1 case of chronic renal failure with uremic encephalopathy and 1 case of acute glomerulonephritis. Acute bacterial meningitis was the cause of seizure in one case. 1 case of seizure occurred in a chronic alcoholic patient because of alcohol withdrawal. Most of the patients were young adults.

In our study, which was conducted in medical wards, hyperglycemic fits was the commonest cause of acute symptomatic seizure. In a study conducted in Minnesota it was found that head injury is the most common (16%) cause of acute symptomatic seizures. Other common causes are stroke (15%), CNS infection (15%), metabolic (9%) drug withdrawal (10%) and eclampsia (2%).

METABOLIC SEIZURES

In our study, 5 patients (12%) had seizures due to metabolic insult. Most common metabolic disorder identified was **nonketotic hyperglycemia**. Non ketotic hyperglycemia constituted about 60% of seizures due to metabolic diseases. Other causes were uremic encephalopathy in a patient with chronic renal failure and a case of acute glomerulonephritis.

Interestingly, all the patients with **nonketotic hyperglycemia** presented with simple partial motor seizures. All of them had postictal paralysis of involved limbs. CT Brain was found to be normal in all these patients. 2 patients were known uncontrolled diabetics and 1 case was a newly diagnosed case. They were in the age group of 55-65 Years. Many studies proved the importance of nonketotic hyperglycemia as a cause of seizures especially in elderly patients.

Seizures associated with nonketotic hyperglycemia were first reported in 1965. Many other reports followed confirming the occurrence of seizures in non ketotic hyperglycemia. Neurologic manifestations such as seizures, postictal focal neurological impairment may provide the first clinical clues to the presence of nonketotic hyperglycemia. Mean age of onset is between 48-72 years.

As a rule, seizures occur when hyperglycemia is not severe and osmolarity is normal or only slightly increased with normal to moderately decreased sodium levels[13]. Commonly, seizures are partial motor seizures occurring in 75-86%. The seizures are frequent and repetitive and often followed by transient postictal paralysis. In nonketotic hyperglycemia cerebral structural lesion has been found in only 15% of cases. Ketotic hyperglycemia is much less frequently associated with seizures, possibly because of the antiepileptic effect of ketosis.

PATIENTS WITH ABNORMAL CT SCAN IMAGING

CT scan directly image the intraparenchymal abnormalities. CT scan proved sensitive for macroscopic pathology associated with epilepsy, (e.g) large destructive lesion and cerebral infarct. CT studies are commonly normal in patients with partial seizures related to microscopic pathology like mesial temporal sclerosis, low grade glioma or cavernous hemangioma.

In our study, 13 patients (31%) had abnormal CT imaging. Most common structural abnormality was ischemic cerebral infarct which was found in 8 patients (61%). 4 patients had space occupying lesions in the brain – 1 case of brain tumour, 1 case of multiple neurocysticercosis, 1 case of calcified granuloma and 1 case of single nodular enhancing lesion. 1 patient had gliosis due to old cerebral hemorrhage.

In this study, out of 8 patients with partial seizures, 5 patients (65%) had abnormal CT imaging. Out of 34 patients with GTCS only 8 patients (24%) had abnormal CT scan imaging. This indicates that patients with partial seizures have more likelihood of having abnormal CT scan than patients with GTCS.

PATIENTS WITH ABNORMAL EEG

EEG is most useful in the investigation and management of patients with epilepsy. The presence of epileptiform activity in the EEG in a patient with suspected epilepsy increases the likelihood that the attacks are indeed epileptic. In patients with established seizure disorder, the EEG finding may help to classify the seizure disorder, identify a focal or lateralized epileptogenic source, provides a guide to prognosis and indicate the most appropriate medication that should be prescribed.

In our study, 8 patients had abnormal epileptiform activity in the interictal EEG. Of these, 7 patients had lateralized sharp wave epileptiform activity and 1 patient had slow wave activity, which suggested a hemispherical lesion. So, EEG was useful in many patients with adult onset seizure to identify a focus of seizure activity.

CONCLUSION

A clinical and diagnostic study including metabolic profile, CT Brain and EEG was done in 42 patients aged more than 25 years with seizures who were admitted in Thanjavur Medical College Hospital between December 2004 to June 2006.

- The maximum incidence occurred in the young adults aged 25-40 years.
- The male to female ratio was 3:1.
- **Generalized tonic clonic seizure** was the most common seizure type observed.
- Most of the seizures (60%) in adults had identifiable etiology.Only 40% of cases were idiopathic without determined etiology by the availabe investigations.
- **Cerebrovascular disease** was found to be the most common etiological factor for seizures in adults.
- All elderly patients aged more than 60 years had identifiable cause for their seizure. Idiopathic seizures were not found in elderly patients.
- **Nonketotic hyperglycemia** was found to be the most common metabolic cause of seizures in adults.
- Other causes of seizures in adults were space occupying lesions, head injury, CNS infection and risk factors for embolic stroke.

- 31% of patients had abnormal CT scan imaging of brain. This suggests the importance of CT scan imaging in adult patients with seizures.
- 19% of patients had lateralizing epileptiform activity in the interictal EEG. This shows the importance of EEG in finding focal lesion in adults with seizure.

A CLINICAL AND DIAGNOSTIC STUDY OF

EPILEPSY IN ADULTS

PROFORMA

Name : Age : Sex :

IP No : Ward : DOA : DOD :

Address :

PRESENTING SYMPTOMS :

History of Seizure :

Aura / Consciousness / tongue bite/ Tonic clonic movements /

injury to body parts / Urinary incontinence / Postictal confusion or headache

First episode or Recurrent seizure :

Type of seizure :

Age of onset of seizures :

Time of recent seizure :

Average frequency of the seizures :

Details of AED (Antiepileptic drugs):

Name of drug Dosage Duration of treatment Compliance.

Precipitating Factors :

Sleep deprivation	fasting	fever	alcohol
Drugs	metabolic factors		Stress

PAST HISTORY :

H/O Neonatal Seizures H/o febrile seizures

Mental retardation

H/O Head injury :

Time since Head injury : Penetrating/Non penetrating :

Duration of LOC : Skull fracture

Brain contusion/ICH :

H/o Neurosurgical Procedure

H/o CNS infection

H/o ICT

H/o Cerebrovascular accident/TIA

H/o MI, Hypertension, DM, ischemic heart disease,
Rheumatic Heart disease

PERSONAL HISTORY :

Smoking :

Alcoholism :

FAMILY HISTORY OF EPILEPSY:

CLINICAL EXAMINATION :

Pallor Icterus facial puffiness

Neurocutaneous markers

BP PR

CVS RS ABDOMEN

CNS - Mental status Examination

Neurological deficit

Signs of meningeal irritation

Fundus

INVESTIGATIONS :

Urine : Albumin Sugar Deposits

Blood : HB TC DC ESR

Sugar Electrolytes

Urea Calcium

Creatinine Liver function tests

ECG Xray Chest PA view

CT Brain

EEG

Remarks :

BIBLIOGRAPHY

1. J. ENGEL and T.A. Pedley - ``Epilepsy` volume – 1 P. 15-37.
2. LENNOX WG. `Epilepsy and related Disorders``. P.532-574.
3. DALE C. HESDORFFER and CHRISTOPHER M. VERITY. ``Epilepsy` 1 Volume-1 P.59-67.
4. DANIEL H. LOWENSTEIN-HORRISON'S principles of Internal Medicine – 16th Edition – Volume. II. P.2357-2372.
5. J.S. CHOPRA and IMS SAWHNEY-Neurology in Tropics- P.527-541.
6. MICHAEL J. AMINOFF – ``Electrodiagnosis in Clinical Neurology`` - 5th Edition – P.131-161.
7. ERNST NIEDERMEYER, M.D. and FERNANDO LOPES DA SILVA. M.D.- Electroencephalography – Basic Principles and clinical applications. 5th Edition – P.505-595.
8. Neuropsychiatric aspects of epilepsy by MARIO F.MENDEZ ASHLA M.D.-Kaplan and Sadock's comprehensive Text Book of Psychiatry. 8th Edition.P.377-390.
9. DAVID SUTTON – Text book of Radiology and Imaging 7th Edition. Volume – 2 P.1804-1805.

10. LAWRENCE N. TANENBAUM, M.D., - Seizure imaging – Orrison's Neuroimaging – Volume, P.917-939.

11. J.M.K. MURTHY – API Text book of Medicine – 7th Edition. P.779-791.

12. JEAN AICARDI and DAVID C. TAYLOR-Epilepsy A comprehensive Text Book-Volume-1 P. 805-809.

13. J.ENGEL and T.A. PEDLEY-Epilepsy-Electrolyte, Matabolic and Endocrine Disorders Volume-III P. 2605-2620.

14. S.D. FANNER-Epilepsy in developing countries-Oct. 1997. 2nd Edition-P. 36-54.

15. JOHN S. DUNCAN-Text Book of clinical Epilepsy-Ist Edition (1995).

16. Adult onset epilepsies-causes-published by The NATIONAL SOCIETY FOR EPILEPSY (NSE)

17. Late onset seizures-published in Epilepsia 42 suppl. 7:143 (Abst. 20, 127) 2001.

18. DAM AM. Late onset epilepsy; etiologies, types of seizures and value of CT scan and EEG, Epilepsia 1985; 26 : 227-231.

19. GUPTA SR, Rubino FA. Post infarction seizures : a clinical study. Stroke 1981; 19 : 1477-1481.

20. HAUSER WA. Seizure disorders, the changes with age (Review). Epilepsia 1992; 33 (Suppl.4) : 56-14.

21. FRANCESCHETTI S : Relationship between tumours and epilepsy, In : Broggi G, ed. The Rational Basis of the surgical treatment of Epilepsies, London. John Libbey; 1988.

22. HAUSER WA, MORRIS ML. Risk for seizures and epilepsy following cerebrovascular insults. Epilepsia. 1984 ; 25 : 666.

23. CAVENESS, W.F. et.al., The nature of post-traumatic epilepsy. J. Neurosurg, 50, 545-553.

24. SHORVON, S.D., et.al., Evidence of Vascular disease from CT scanning in later onset epilepsy. J.Neurol. Neurosurg. 47, 225-230.

25. CALAL. A, WOODING T.C. Computerized Tomogram of the cranium in patients with epilepsy. Epilepsia 1996; 32nd Volume, Pages; 23-27.